Ethnic Disparity in Diabetes: The Role of Gender, Insulin, and Obesity

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Patient 1

- 45 year old woman, BMI 24
- BP 138/86
- Fasting Insulin 111
- Total Cholesterol 206, TGs 200, HDL 40, LDL 126
- *Normal Weight, with Metabolic Syndrome*
- *"Metabolically Obese, Normal Weight" (Ruderman, 1998)*

Patient 2

- 45 year old woman, BMI 34
- BP 128/76
- Fasting Insulin 98
- Total Cholesterol 206, TGs 130, HDL 50, LDL 130
- *Obesity, without metabolic syndrome*

Does Obesity operate differently in different groups?

- Ethnic minorities have higher prevalence of obesity
- Ethnic minorities have higher prevalence of Type II diabetes and CHD
- The excess diabetes and CHD is not fully explained by the excess obesity
- Is there an interaction?

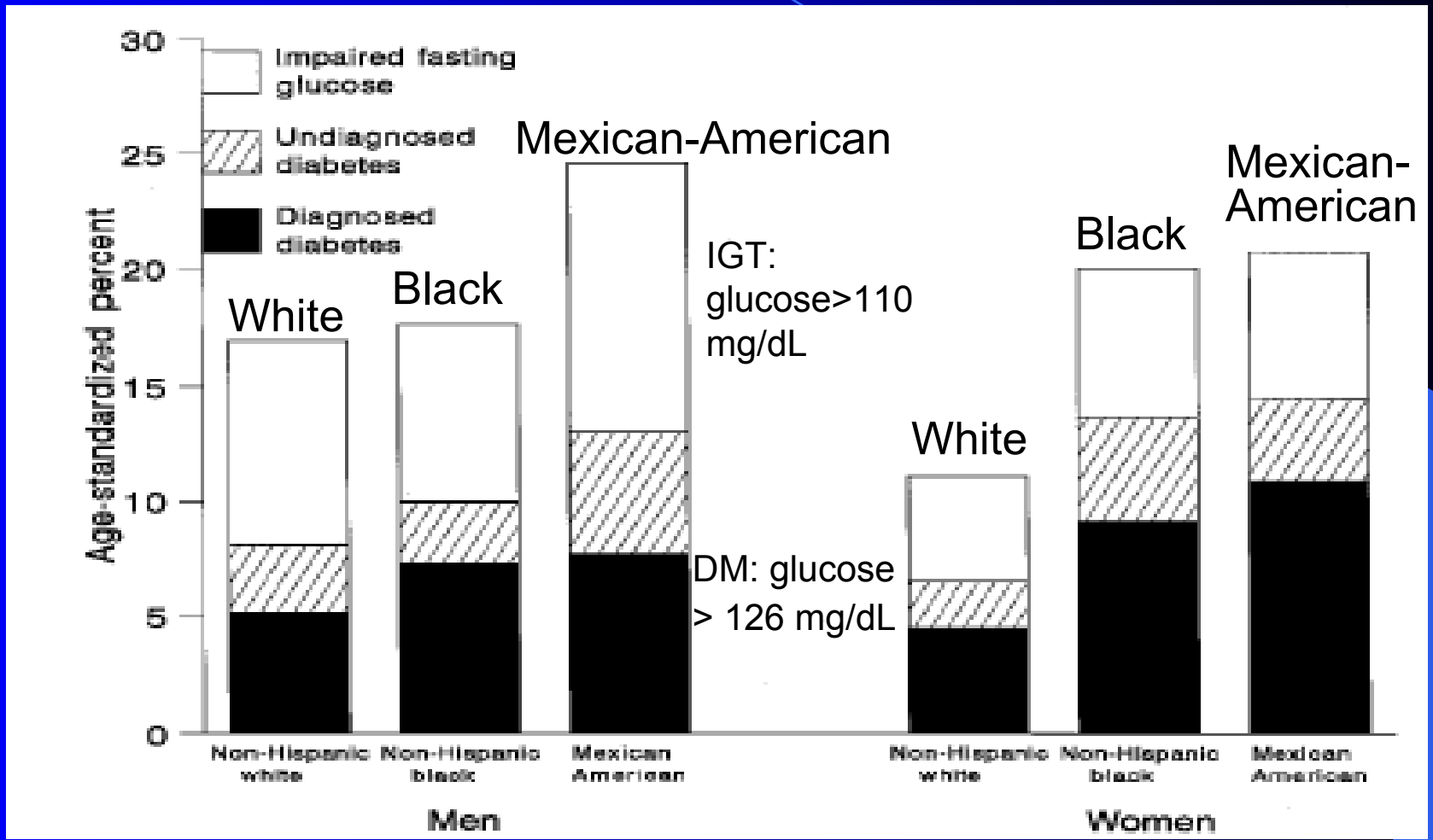
Background

- Excess prevalence of Type II diabetes in ethnic minorities. (Brancati, *JAMA* 2000; 283: 2253)

- Physical inactivity, obesity, and low SES partially explain the ethnic disparity
  - Joint combination only explains half the excess(Brancati, *JAMA* 2000; 283: 2253)

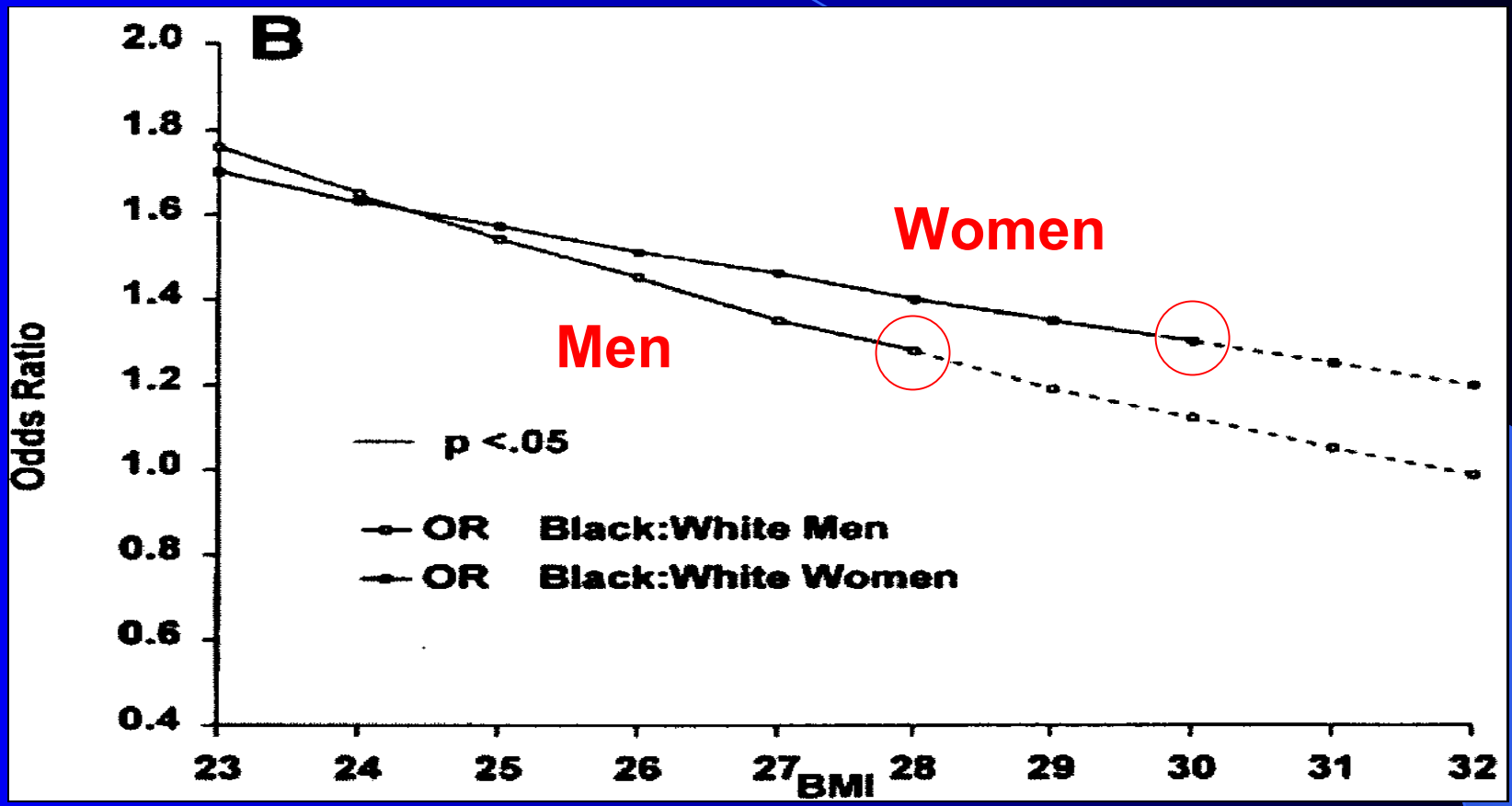
- Both hyperinsulinemia and obesity are known risk factors.

Ethnic Disparity in Diabetes



Harris et al. *Diabetes Care* 1998; 21 (4): 518

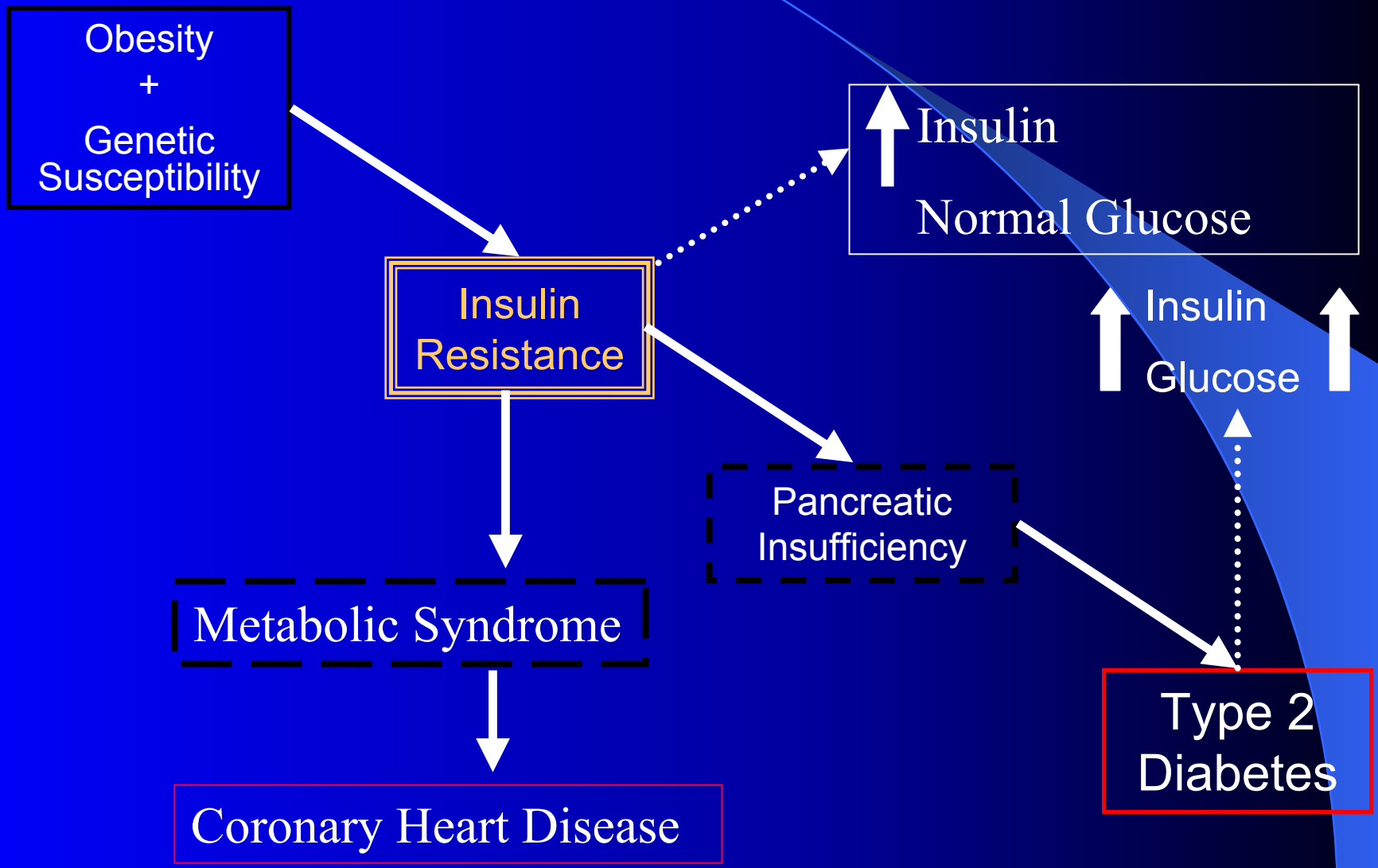
Odds Ratio of Diabetes by Gender and BMI



Differential Effects of BMI on Diabetes Risk Among Black and White Americans: NHEFS I

Resnick: *Diabetes Care*, 1998; 21: 1828

Role of Insulin Resistance



Metabolic Syndrome

1) Abdominal obesity: waist circumference >102 cm in men and >88 cm in women
2) Hypertriglyceridemia: >150 mg/dL (1.69 mmol/L)
3) Low high-density lipoprotein (HDL) cholesterol: <40 mg/dL (1.04 mmol/L) in men and <50 mg/dL (1.29 mmol/L) in women
4) High blood pressure: >130/85 mm Hg
5) High fasting glucose: >110 mg/dL (6.1 mmol/L)

Metabolic syndrome is defined as any three of the above.

Insulin Resistance in Ethnic Minorities

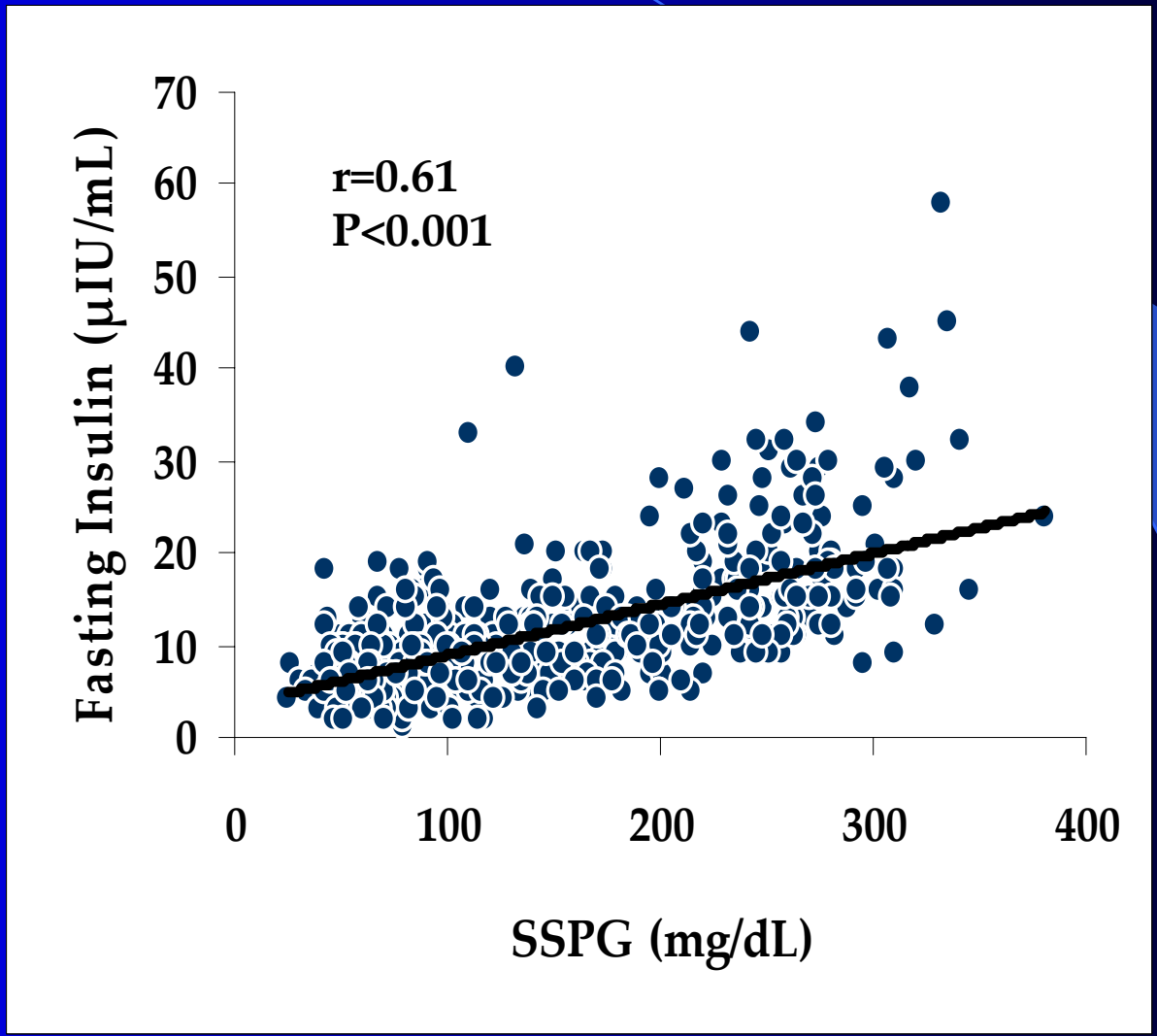
- Fasting and post-challenge insulin higher among black children (aged 5 – 10) compared to white children

  (Gower, *Am J Clin Nutr* 1998; 67: 821)
- Insulin sensitivity index lower among black women compared to white women

  (Lovejoy, *Metabolism* 1996; 45: 1119)
- Insulin sensitivity lower among non-diabetic black and Hispanic adults (aged 40-69) than whites, IRAS Study

  (Haffner, *Diabetes* 1996; 45: 742)

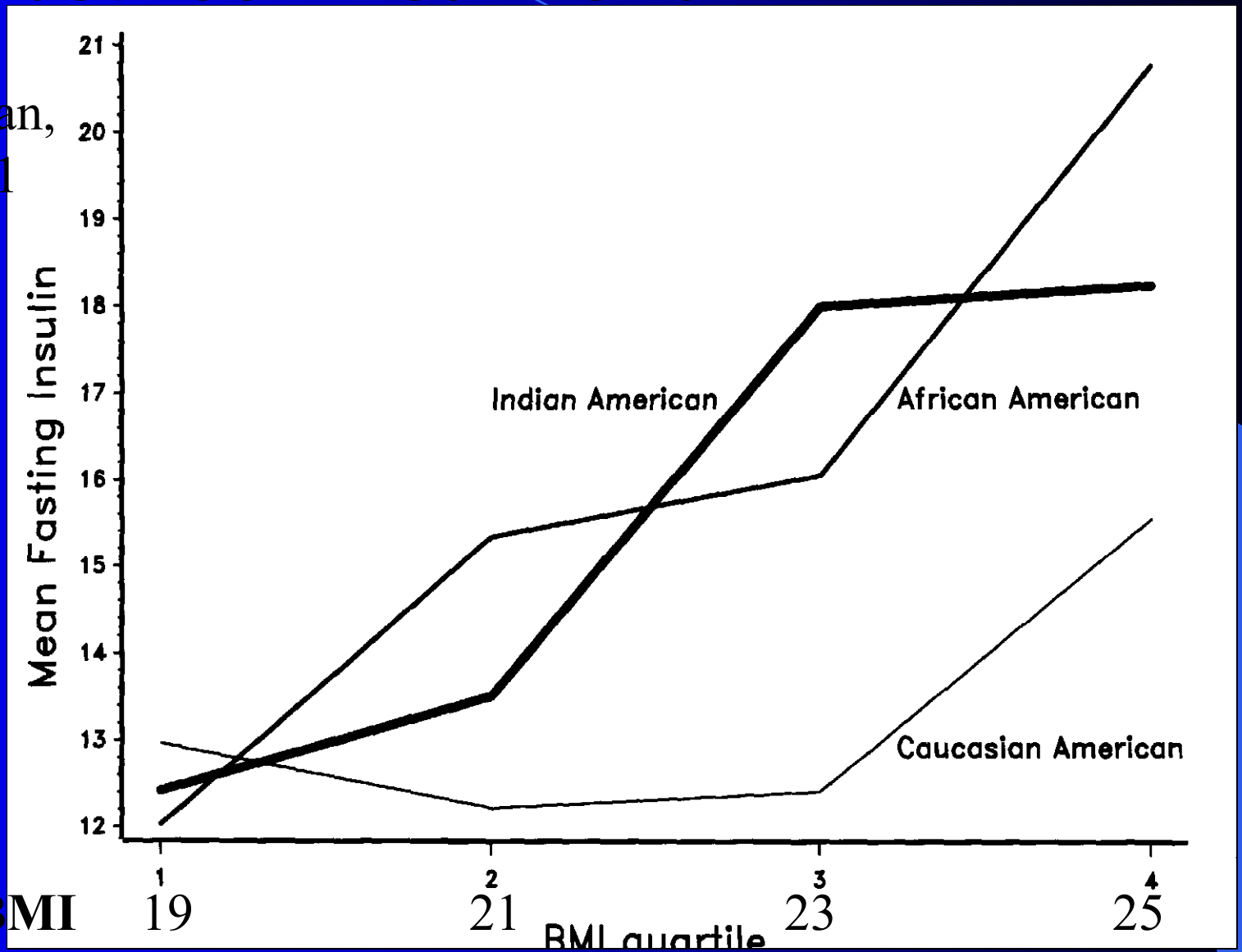
Relationship Between Insulin Resistance (SSPG Concentration) and Fasting Insulin Levels in 490 Nondiabetic Subjects



Komshian H. *Diabetes Care.* 2000;23:171-175

Ethnicity modifies the interaction between insulin and BMI

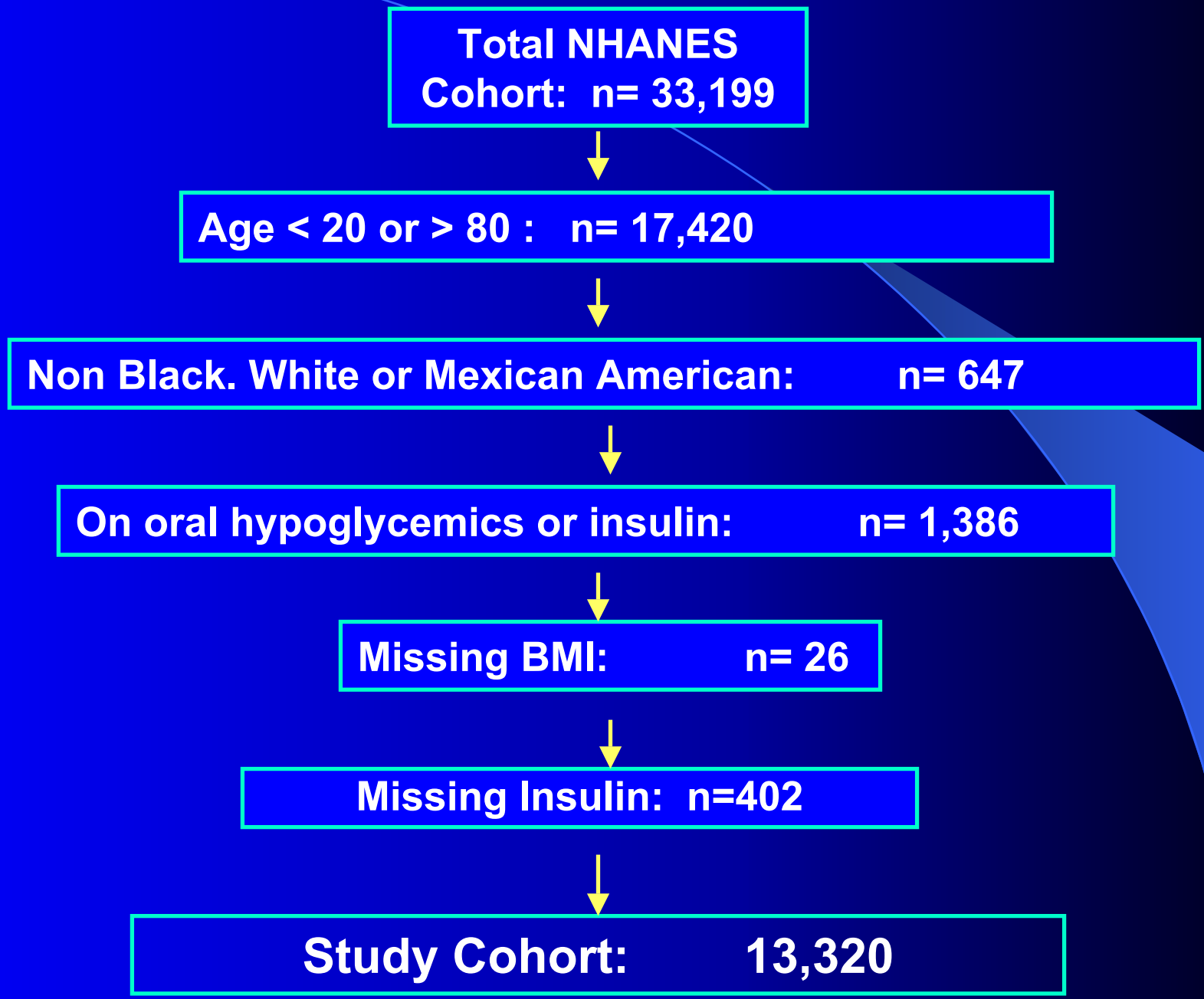
Palaniappan, et al., 2001



Does the relationship between obesity and insulin differ between Black, Mexican American and White adults?

NHANES III 1998-1994

- Many areas
- Cross sectional
- Lots of participants
- Men and Women
- Age 20-80
- Three ethnicities, Black, White & Mexican American


Total NHANES
Cohort: n= 33,199
Age < 20 or > 80 : n= 17,420
Non Black. White or Mexican American: n= 647
On oral hypoglycemics or insulin: n= 1,386
Missing BMI: n= 26
Missing Insulin: n=402
Study Cohort: 13,320

Fasting Insulin and BMI

- Fasting (> 8 hours) blood draw at baseline
  - Serum insulin concentration
- Body Mass Index (BMI)
  - Weight (kg)/Height (meters)^2

Obesity: BMI $\geq$ 30

Overweight: BMI $\geq$ 25

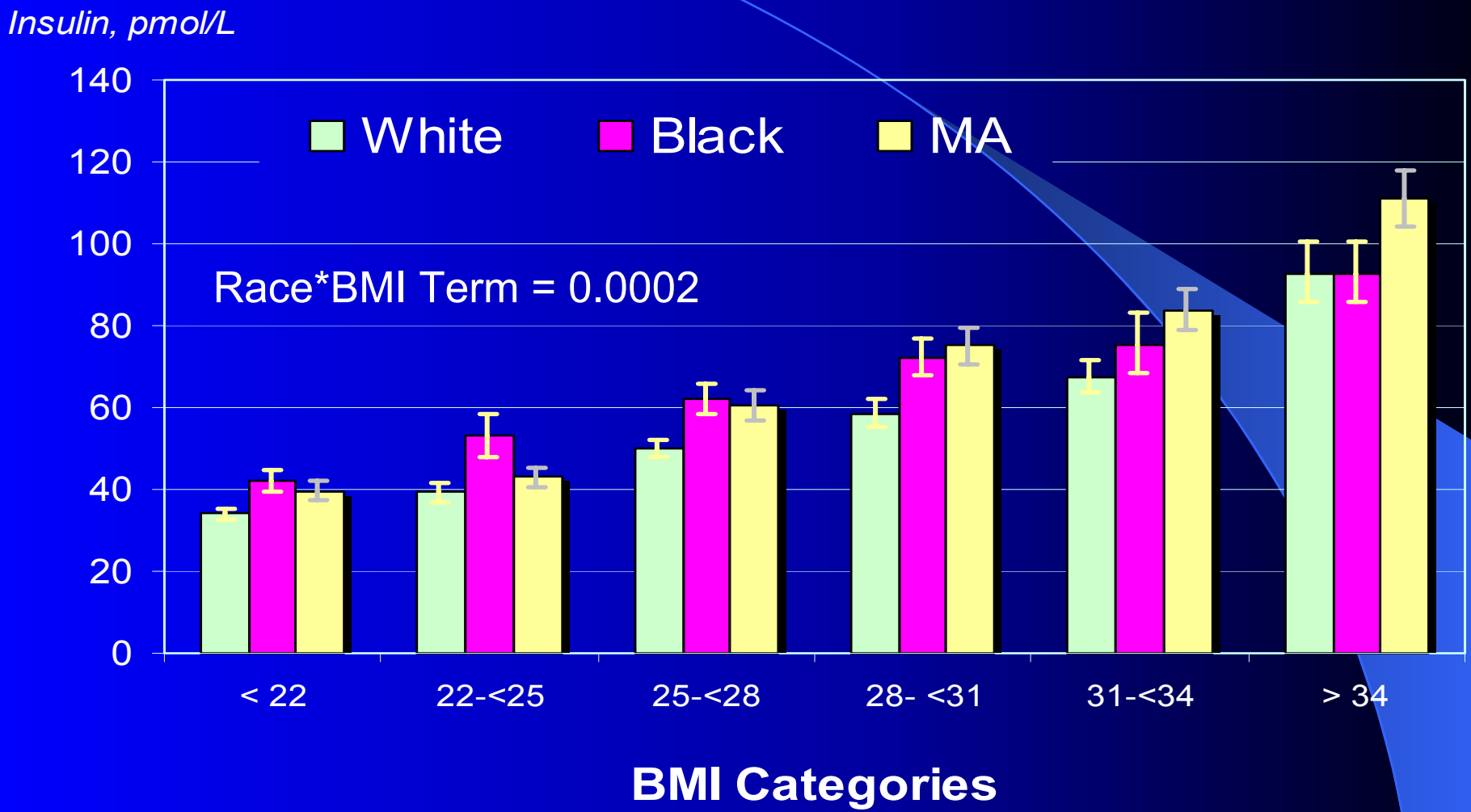
Demographics: Women

	Non-Hispanic White N=3,026	Non -Hispanic Black N=2,242	Mexican American N=1,997
Age (years)	49.6 ± 17.9	41.2 ± 15.7	39.8 ± 15.4
Education (years)	12.5 ± 2.7	11.7 ± 2.9	8.9 ± 4.4
Household Income<$20K	33.8	57.8	58.3
BMI (kg/m^2)	26.3 ± 6.0	28.8 ± 7.3	27.9 ± 6.0
Obese (BMI > 30), %	23	36.5	30.9
Insulin (pmol/L)	9.7 ± 6.8	13.5 ± 11.6	12.7 ± 10.6

Demographics: Men

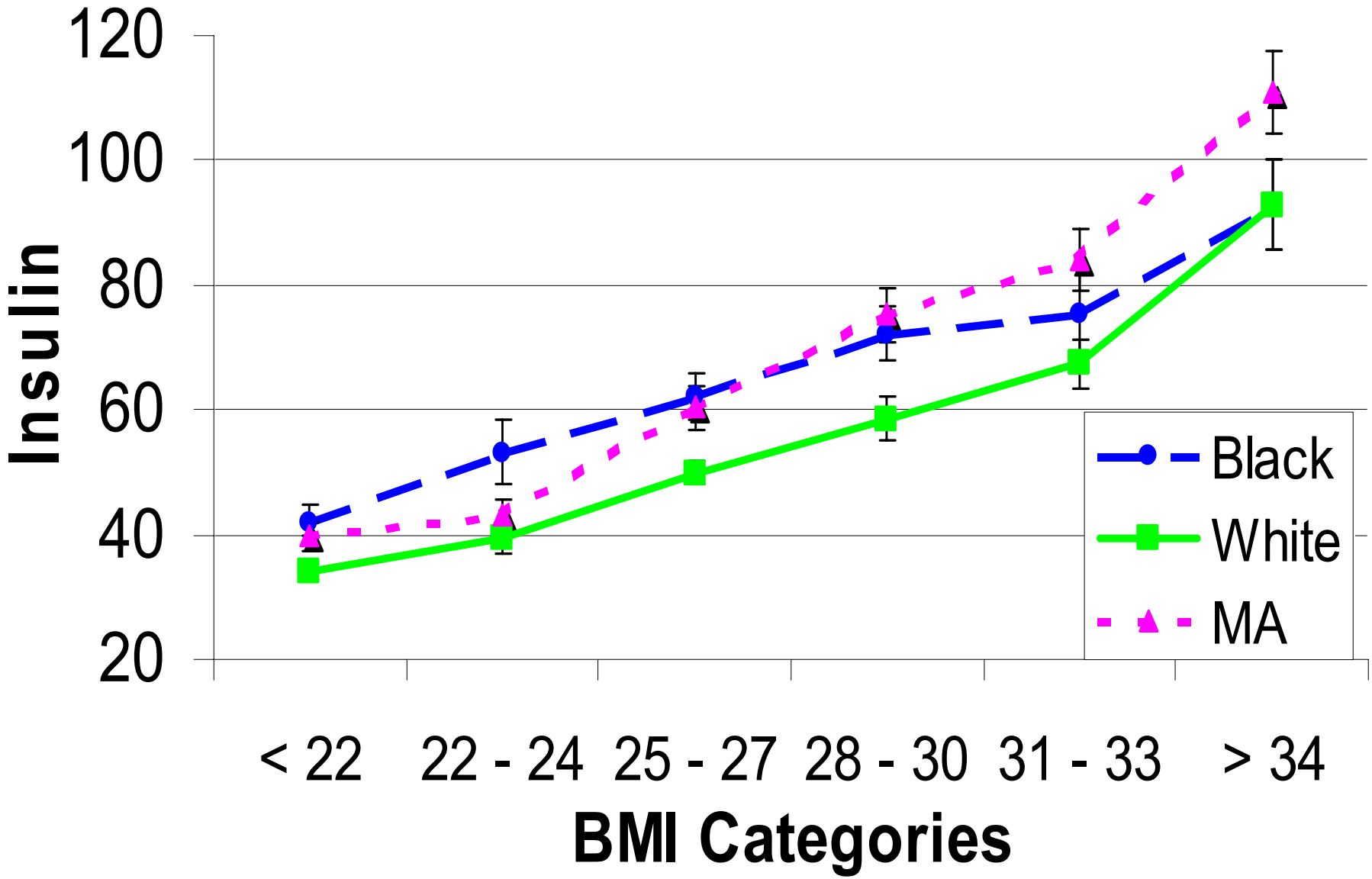
	White N=2,583	Black N=1,881	MexicanAmerican N=2,017
Age (years)	50.7 ± 17.5	43.0 ± 16.4	40.6 ± 16.1
Education (years)	12.6 ± 3.1	11.2 ± 3.4	8.5 ± 4.5
Household Income<$20K	28.4	53.6	57.8
BMI (kg/m^2)	26.7 ± 4.7	26.4 ± 5.4	27.0 ± 4.5
Obese (BMI > 30), %	19.5	19.8	21.5
Insulin (pmol/L)	10.5 ± 8.2	11.5 ± 10.4	12.0 ± 10.7

Mean Insulin by Ethnicity and BMI: Women



Palaniappan LP, Carnethon MR, & Fortmann SP. *Diabetes Care*, December 2001

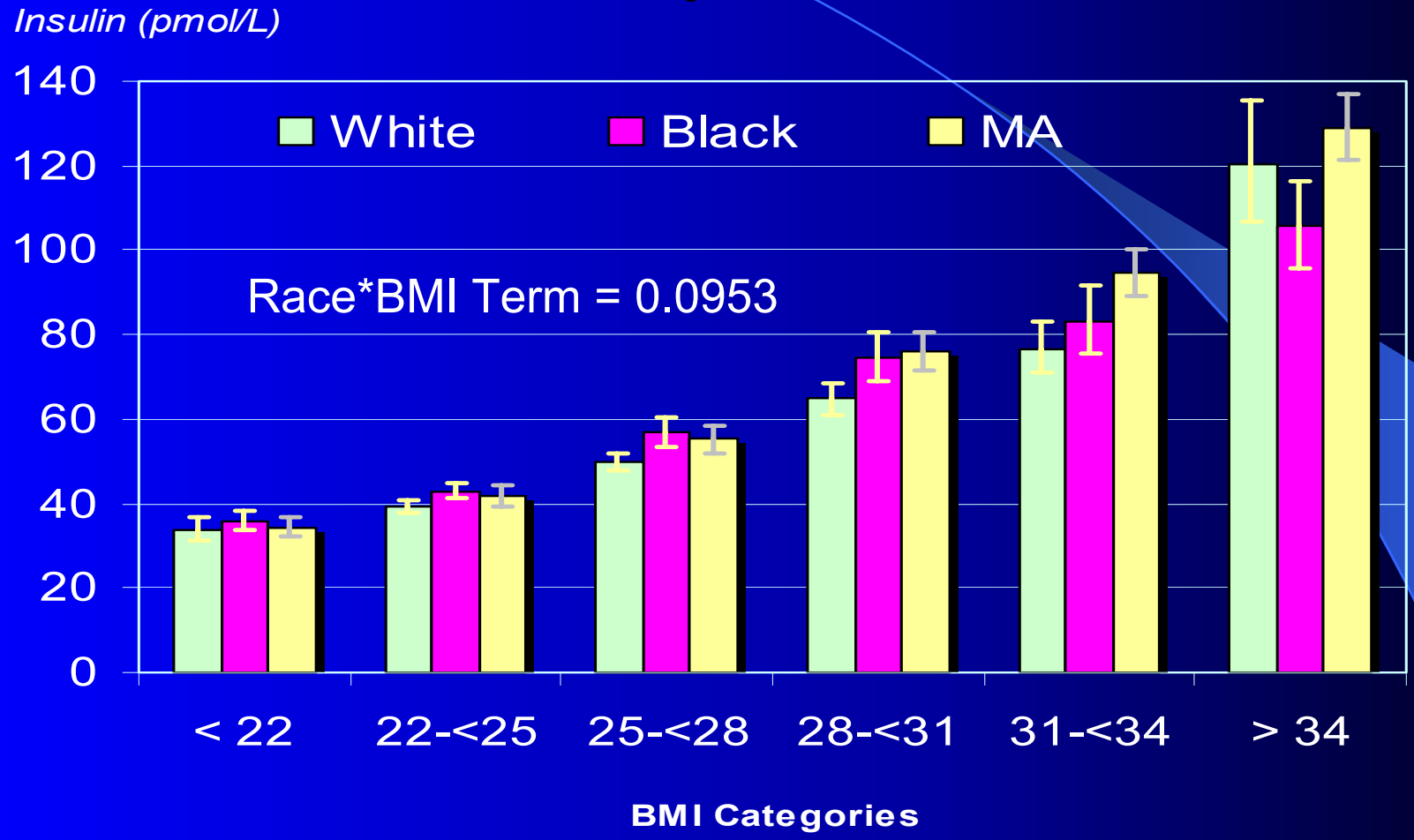
Insulin by Ethnicity - Women



Ethnicity * BMI remains significant after controlling for:

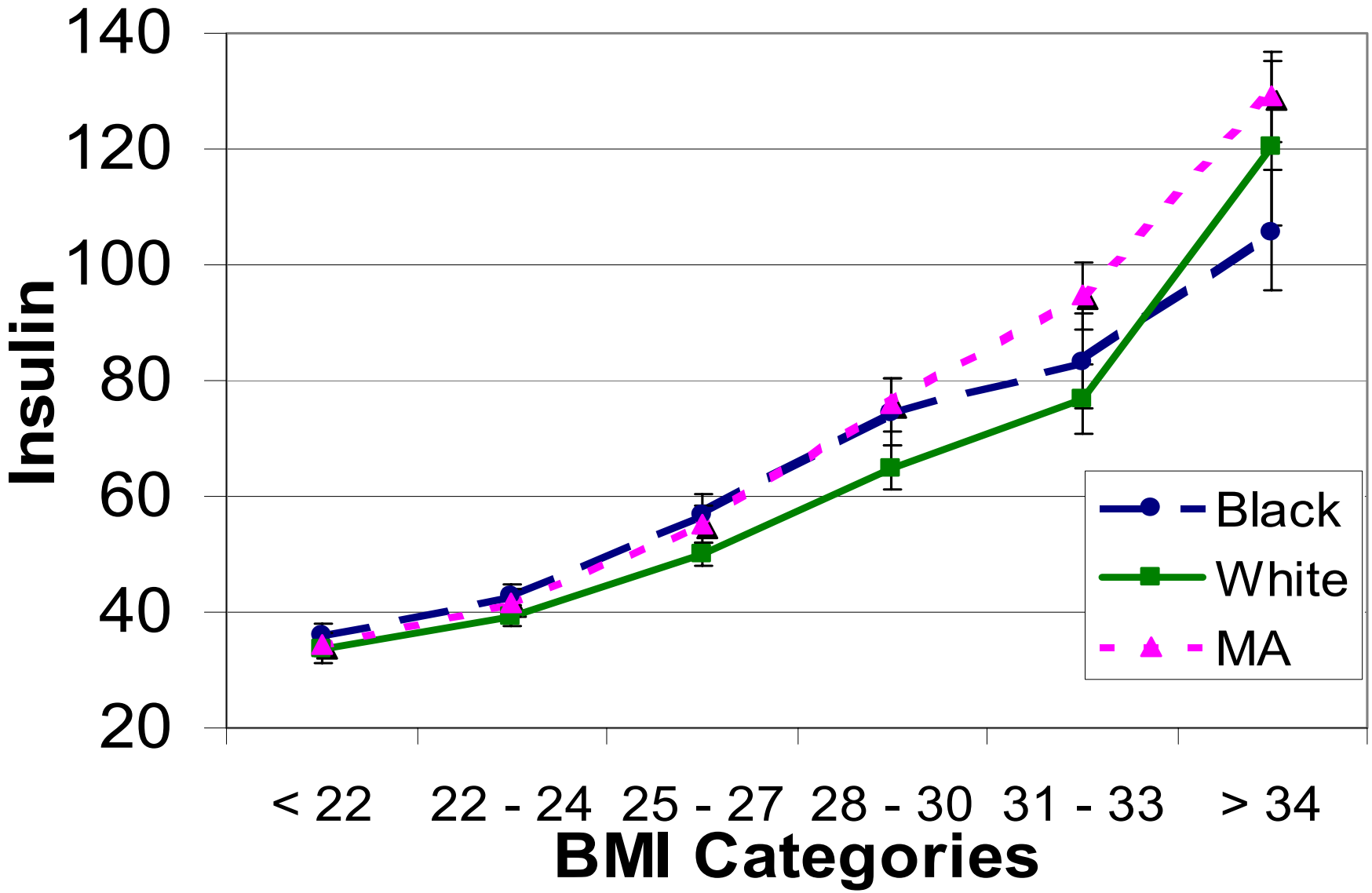
- Diabetes
- Education
- Income
- Physical Activity
- % of calories from carbohydrate
- Age
- Family History of Diabetes

Mean Insulin by Race and BMI: Men



Palaniappan LP, Carnethon MR, & Fortmann SP. *Diabetes Care*, December 2001

Insulin by Ethnicity – Men



Type II Diabetes Clinical Phases

Glucose normal, insulin elevated

Glucose slightly elevated, insulin elevated

Glucose very elevated, insulin decreases

Objective

To determine whether fasting insulin at a lower body weight is an equally important predictor of diabetes in black and white men and women

Atherosclerosis Risk in Communities Study (ARIC)

- Longitudinal study of atherosclerosis and CHD risk factors in approx. 16,000 adults from 4 US communities
- Black and white men and women aged 45-64 at baseline (1987-1989)
- Comprehensive risk factor data collected at baseline clinic examination
- Clinic re-examination in ’96-’98
  - (approx. 10 years follow-up)

Exclusions

	N
Exclusions	**Total Cohort: 15,792**
Non black/white	103
Missing insulin	151
Missing BMI	25
Prevalent diabetes	1,863
BMI < 18.5	130
Total	**13,287**

Sample Size

	N
White Women	5,395
Black Women	1,930
Total Women	**7,325**
White Men	4,757
Black Men	1,205
Total Men	**5,962**

Incident Diabetes Definition

- American Diabetes Assocation defintion: Fasting serum glucose > 126 mg/dL; non-fasting glucose > 200 mg/dL
- Diabetes medication use
- Self-reported physician dx

Baseline Characteristics by Race: Women

	White†	Black
Age (years)	53.8	52.9*
< High School Education, %	15	37*
BMI (kg/m^2)	**26.2**	**30.2***
Obese (BMI > 30), %	21	44*
Waist/Hip Ratio	0.89	0.90*
Insulin (pmol/L)	**66.9**	**104.6***
Current Smoking, %	25	26
Physical Activity (1-low; 5-high)	2.4	2.1*

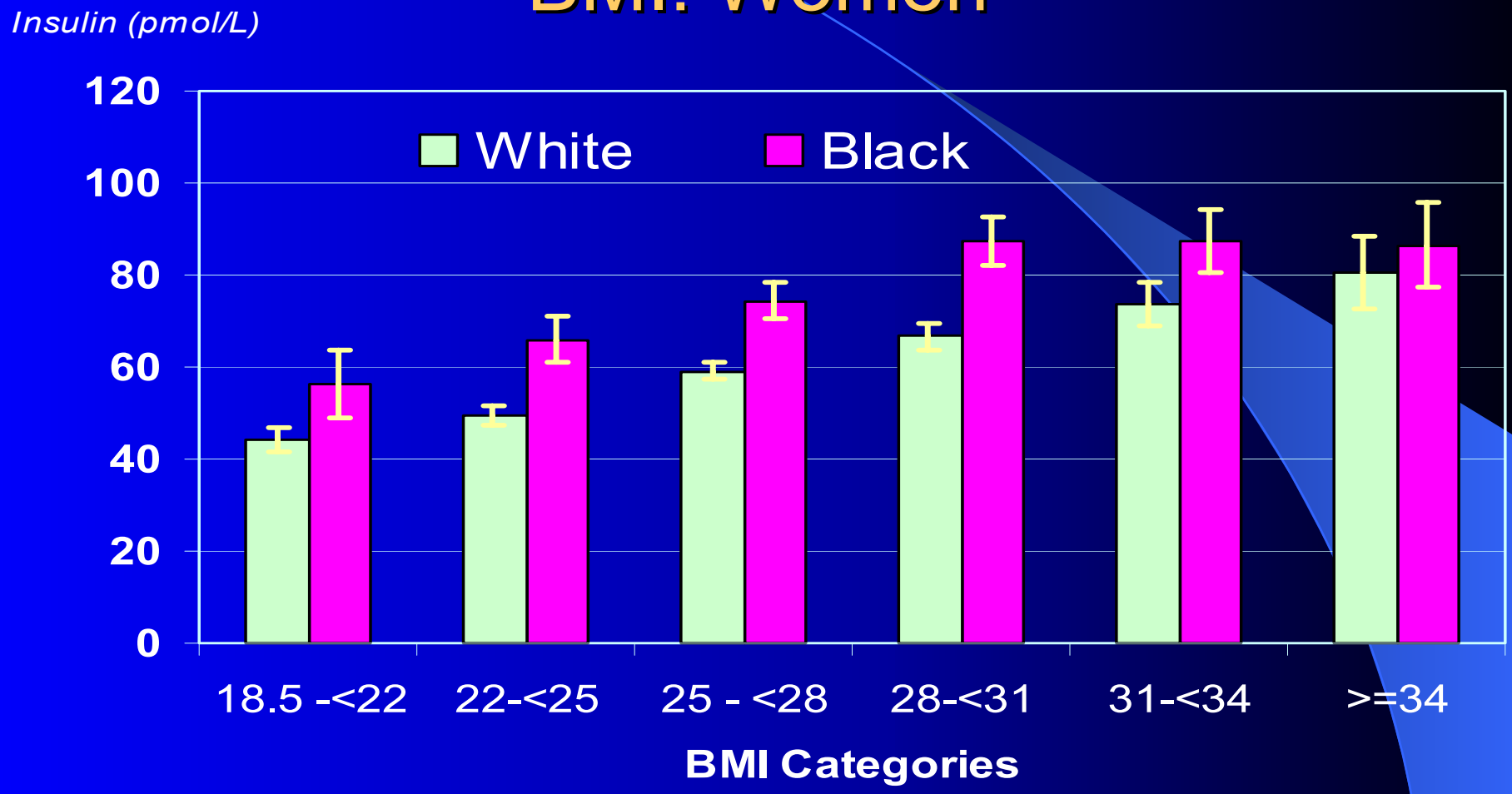
* P < 0.0001 † Referent

Baseline Characteristics by Race: Men

	White †	Black
Age (years)	54.7	53.7*
< High School Education, %	17	43*
BMI (kg/m^2)	**27.2**	**27.2**
Obese (BMI > 30), %	20	24
Waist/Hip Ratio	0.97	0.94*
Insulin (pmol/L)	**79.3**	**80.6**
Current Smoking, %	24	38*
Physical Activity (1=low; 5=high)	2.7	2.3*

* P < 0.0001 † Referent

Adjusted* Mean Insulin by Race and BMI: Women

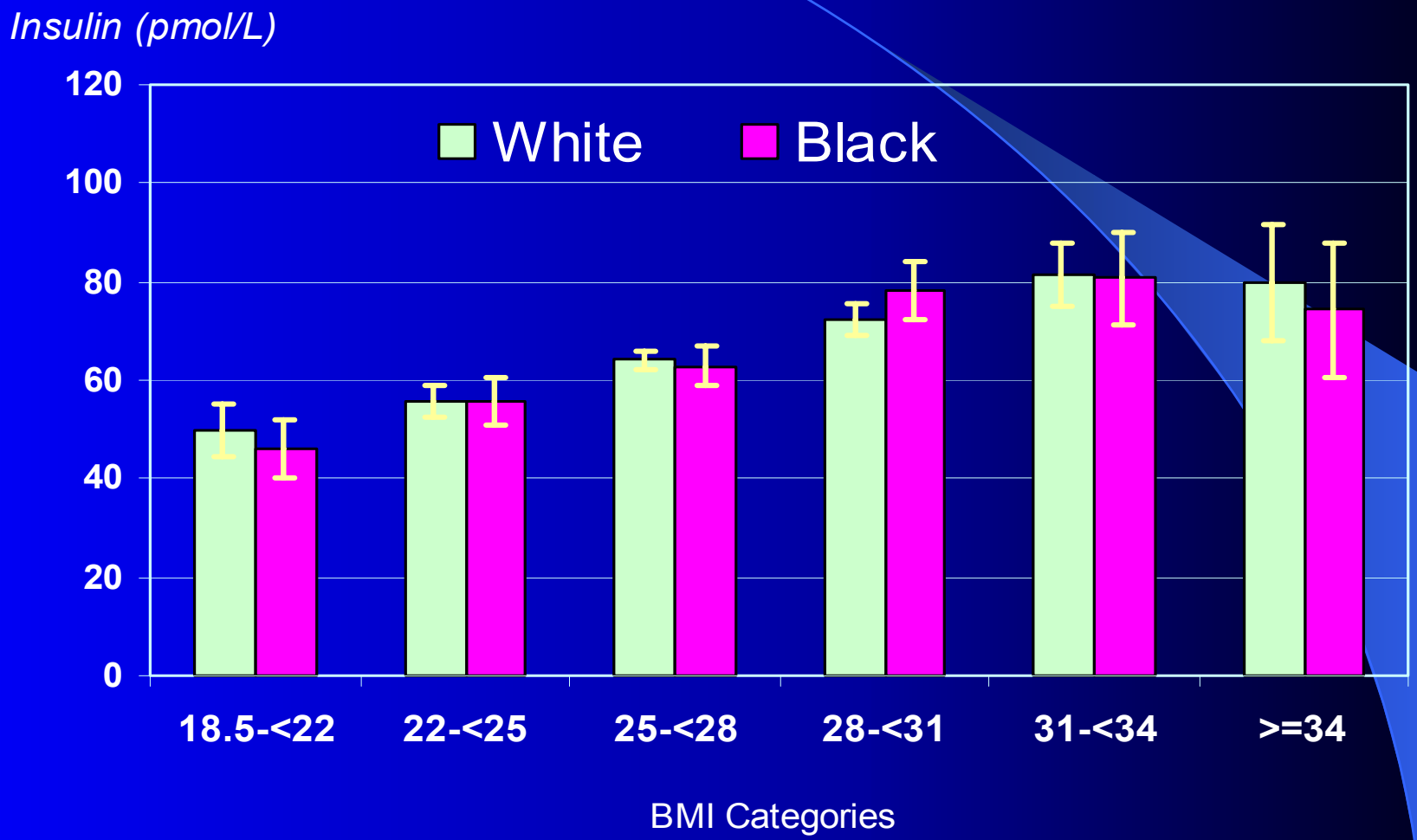


P value from race*BMI interaction term = 0.0003

*** Adjusted for BMI (per 1 unit)**

The ARIC Study

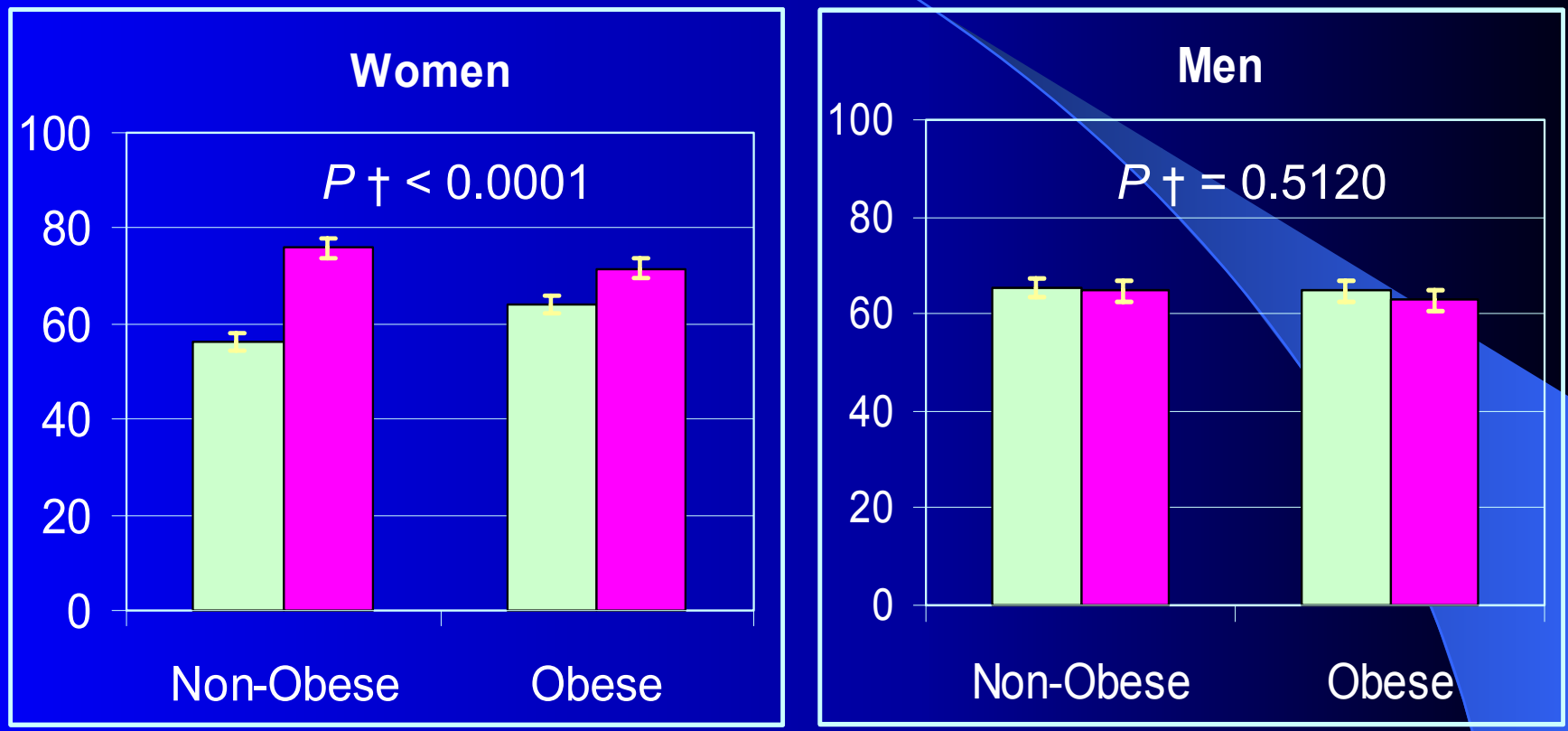
Adjusted* Mean Insulin by Race and BMI: Men



P value from race*BMI interaction term = 0.2626

***Adjusted for BMI (per 1 unit)**

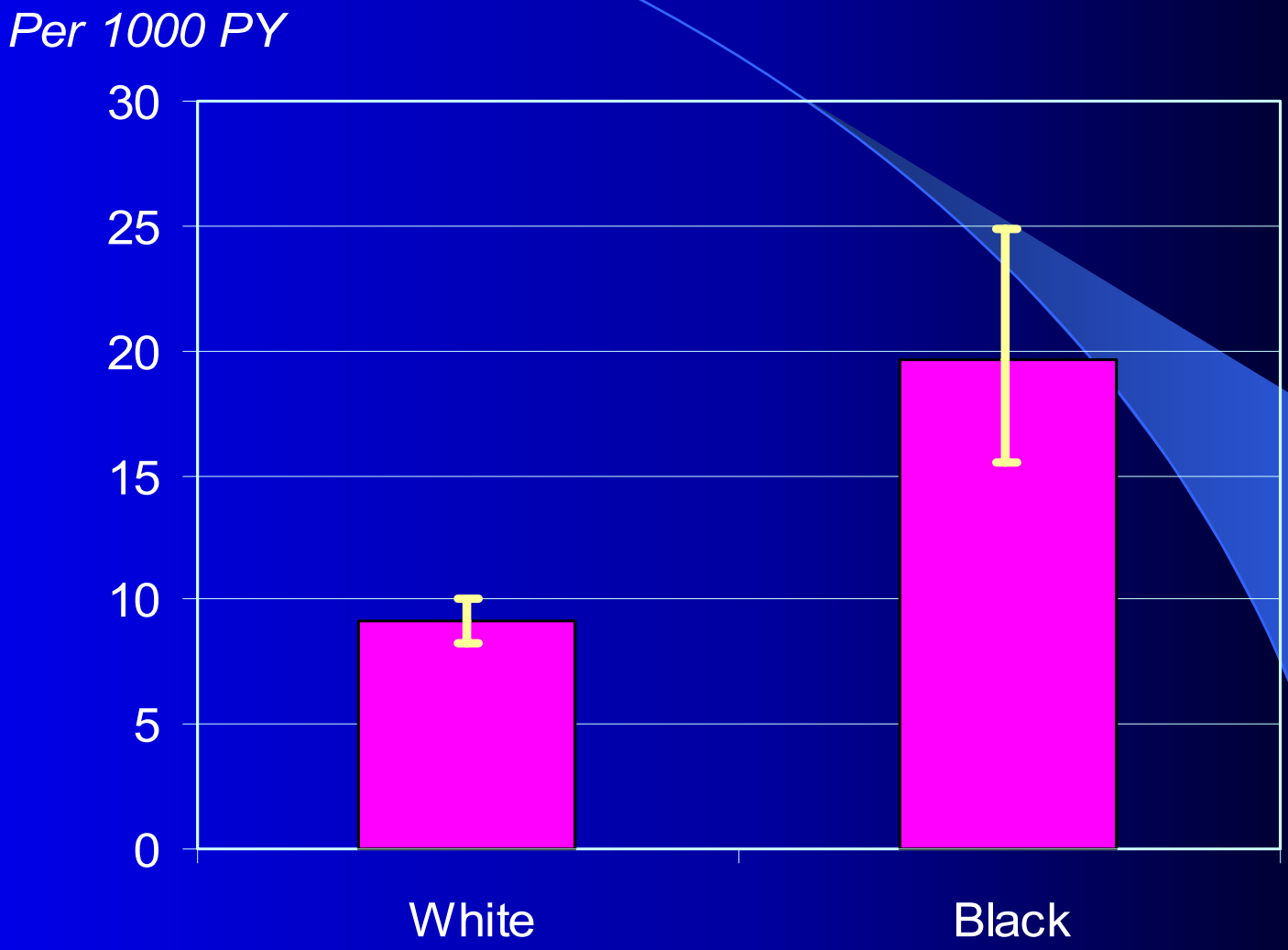
Adjusted* Mean Insulin by Obesity Status and Race



* Adjusted for BMI (per 1 unit)

† P-value from Race*Obesity interaction term

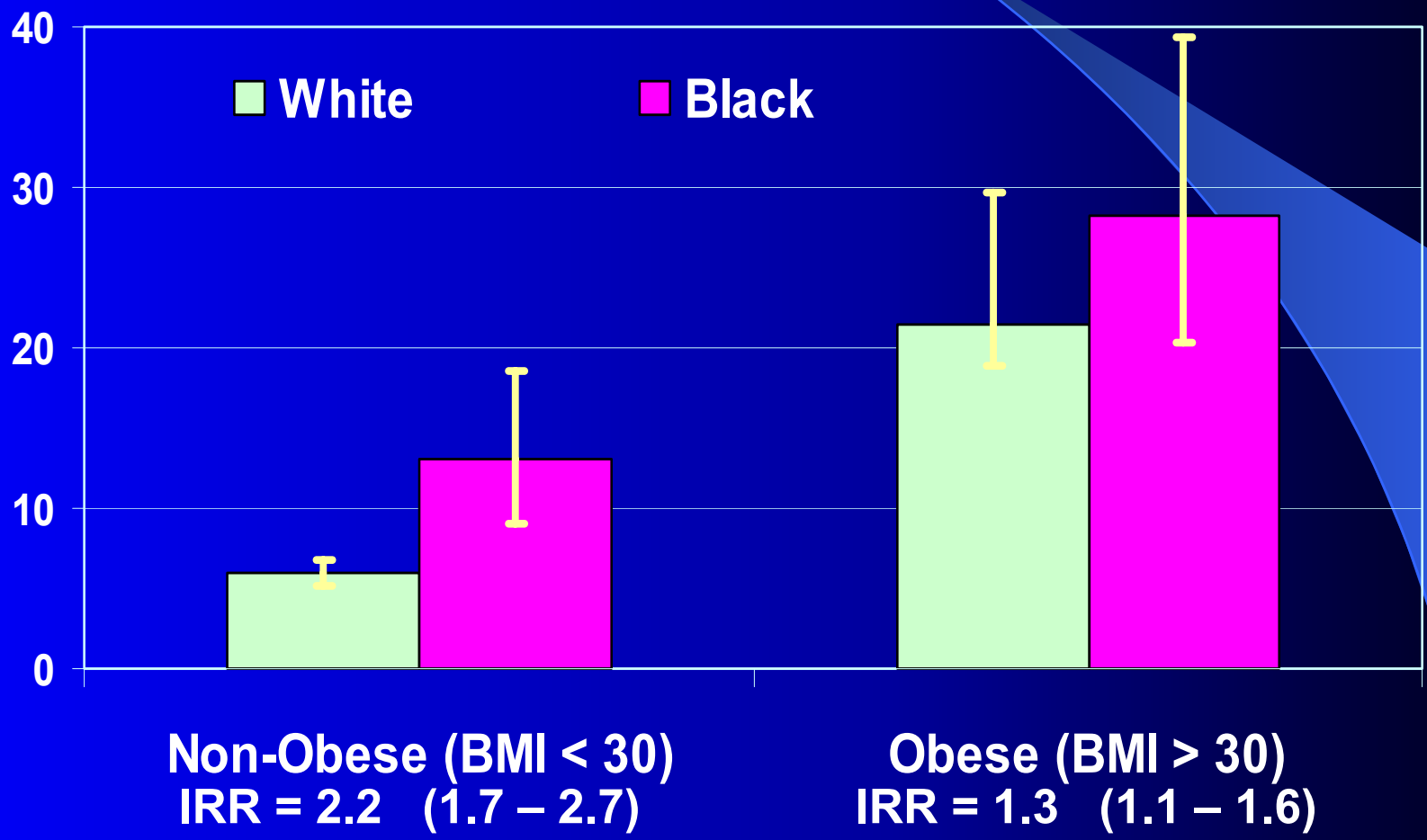
Incidence Rate of Diabetes per 1000 Person-Years: Women



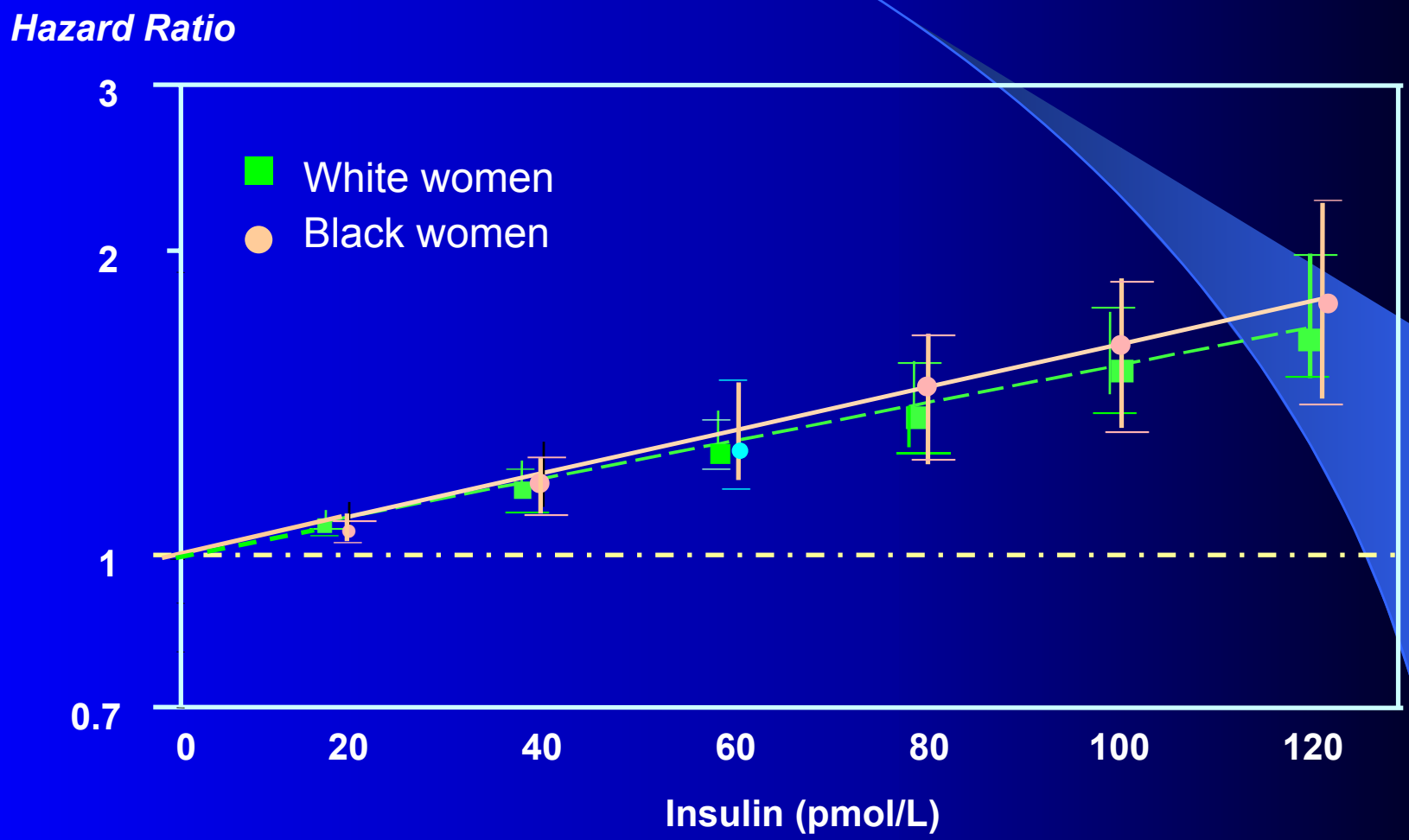
Incidence Rate Ratio (IRR) = 2.2 (1.9 – 2.5), $p < 0.0001$

Incidence Rate of Diabetes by Obesity Status: Women

Per 1000 PY



Adjusted Hazard Ratios of Incident Diabetes by Fasting Insulin: Non-Obese (BMI < 30) Women



Race*Insulin Interaction Term: p=0.6273

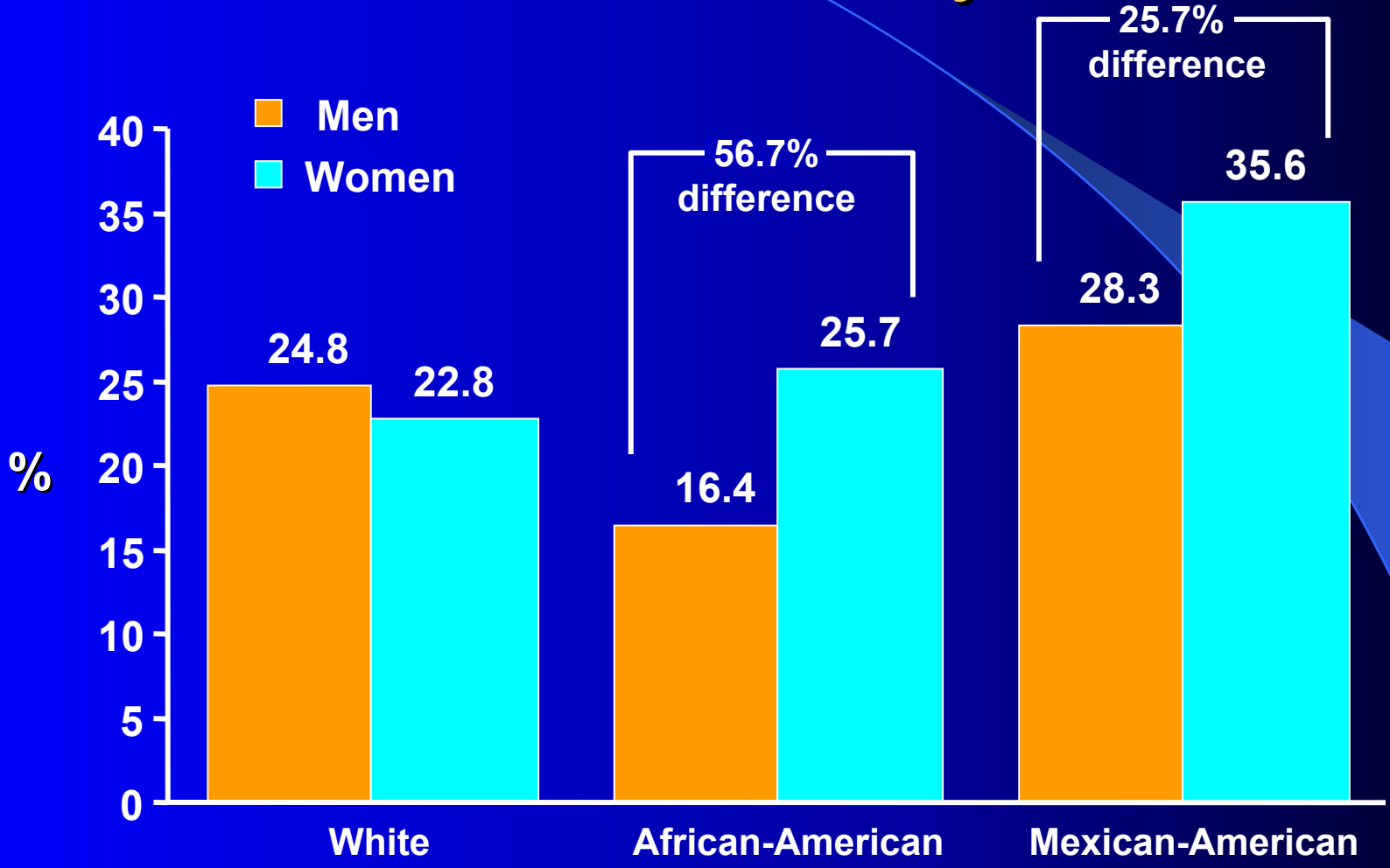
Summary

- Fasting insulin higher among ethnic minority women than white women at a lower body mass
- Differences not as apparent among men
- Fasting insulin is a strong predictor of diabetes among non-obese (BMI < 30) women
- **High fasting insulin is an equally strong predictor among non-obese black and white women**

Why Women? (more than men)

- Striking disparity in obesity between black and white women not found for men (Kumanyika, 1994)
- Lower 24-hour energy expenditure among black women compared to white; no differences among men (Weyer, 1999)
- Insulin inhibits the breakdown of fat stores; women more sensitive to this effect (Sumner,1999)
- Mexican American women are more likely to have impaired glucose tolerance and diabetes than men. (Ramachandran, 1997)

Gender Disparity in the Prevalence of the Metabolic Syndrome



*Criteria based on ATP III; diabetics were included in diagnosis; overall unadjusted prevalence was 21.8%.

Data from Ford ES et al. *JAMA*. 2002;287:356-359.

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Residual Confounding

Residual confounding by socioeconomic status (SES)

Residual confounding by physical activity

BMI as a marker of adiposity

- Waist to Hip ratio was consistent, but other markers of central obesity may be more important

Why Study Ethnic Differences?

- Describe ethnicity-associated differences in health outcomes
  - Excess incidence of diabetes among blacks
- Investigate differences
  - Insulin resistance at a lower body weight
- Interpret ethnic differences
  - Insulin resistance as an explanation for diabetes disparity among non-obese

Kaufman and Cooper 2001 *AJE*; 154: 291 and Jones 2001, *AJE*: 154: 299

Ethnicity and Health Outcomes

- Ethnicity is a strong predictor of health outcomes
- Ethnicity represents differences between social, political, and economic experience
  - NOT a surrogate for genetic factors
  - NOT a biological determinant
- Less advantaged have more detrimental behaviors

Future Studies

- Insulin Resistance Atherosclerosis Study (IRAS) – to study the relationship between ethnicity, obesity, and insulin sensitivity longitudinally in three ethnic groups
- Coronary Artery Risk Development in Young Adults (CARDIA) - To study these relationships in two ethnicities in a younger cohort followed over a longer period of time. (15 years)

Clinical Significance

- May redefine obesity/overweight for ethnic minority populations
- Will raise clinical suspicion for “normal weight” individuals at risk
- Will instigate further research into why these gender differences exist

Thank You!